Public Citizen

Buyers Up • Congress Watch • Critical Mass • Global Trade Watch • Health Research Group • Litigation Group
Joan Claybrook, President

October 29, 2004

Lester Crawford, DVM, Acting Commissioner
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20854

Dear Dr. Crawford,

We have just completed an analysis of the FDA's adverse drug reaction database (AERS) and have found that the rate of reports to the FDA of acute renal failure or renal insufficiency per million prescriptions in patients using rosuvastatin (Crestor)---29 U.S. reports in less than one year since the drug was first marketed in this country---is approximately 75 times higher than the rate for all other statin drugs combined. This letter is a supplement to our petition of March 4, 2004, to ban this drug in the United States.

The concern about acute renal failure was expressed by an FDA medical officer in the July 2003 FDA hearing preceding the approval of the drug. FDA documents discussed during the hearing stated, in the context of dozens of patients with blood and/or protein in their urine after using Crestor and several cases of acute renal failure or renal insufficiency, that:

"These three cases of renal insufficiency of unknown etiology are of concern because they present with a clinical pattern, which is similar to the renal disease seen with rosuvastatin in these clinical trials. ... Proteinuria and hematuria could be potentially managed with regular urinalysis screening. However, if they are the signals for the potential progression to renal failure in a small number of patients, this may represent an unacceptable risk since currently approved statins do not have similar renal effects." [1]

The results contained in our analysis are based on the most recent adverse reaction data available from the FDA for statins other than Crestor (reactions filed between January 1, 2001, and September 30, 2003), and all data on adverse reactions to Crestor from the time of its approval through August 26, 2004, combined with data

[1] FDA Briefing Documents for 7/9/03 Advisory Committee Hearing Page 34.

2004-612

on prescriptions filled in the United States for these same intervals. We did not include cases of acute renal failure or renal insufficiency in which rhabdomyolysis had been diagnosed since this statin-induced adverse reaction can frequently cause renal failure and we only counted cases reported from the U.S. and only those cases in which the adverse drug reaction report stated that Crestor was the "primary suspect" drug related to the adverse reaction.

Crestor: There have been 29 reported cases of acute renal failure or renal insufficiency (18 cases of failure and 11 cases of renal insufficiency) out of 4.5 million prescriptions filled between the first time the drug was marketed in the U.S. – September 2003 – and the end of August 2004. This is a rate of 6.4 reports of acute renal failure or renal insufficiency per million prescriptions filled.

All other statins (Lipitor, Zocor, Lescol, Pravachol and Mevacor, including other versions of lovastatin): There have been 27 cases of acute renal failure or renal insufficiency reported from January 1, 2001, through September 30, 2003, out of 316 million prescriptions filled for these drugs during this interval. This is a rate of 0.085 cases reported per million prescriptions filled. The highest rate for any of these other statins was for Zocor, which had a rate of 0.26 cases per million prescriptions filled.

Thus, the rate of reports of acute renal failure or renal insufficiency for Crestor is 6.4/.085, or 75 times higher than that of all of the other statins combined. In comparison to Zocor, the rate of reports of acute renal failure or renal insufficiency for Crestor is 6.4/.26, or 25 times higher than that of Zocor.

Based on less than one full year of adverse reaction reports of acute renal failure or renal insufficiency, it appears that the concerns of the FDA medical officer cited in the above briefing document were extraordinarily prescient: "However, if they [blood and protein in the urine] are the signals for the potential progression to renal failure in a small number of patients, this may represent an unacceptable risk since currently approved statins do not have similar renal effects."

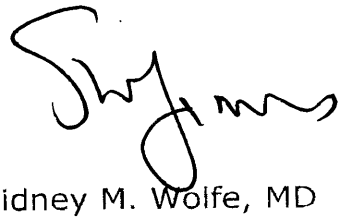
We based our opposition to the approval of this drug on its unique renal toxicity and on the higher rate of life-threatening rhabdomyolysis (destruction of muscle) than had been seen with other statins in pre-approval clinical trials. Seven cases of rhabdomyolysis had shown up in clinical trials prior to the approval

of Crestor, compared to no cases for any of the other statins, including the ultimately doomed Baycol.

As of August 26, 2004, there had been 65 U.S. reports of rhabdomyolysis among patients taking Crestor in less than the first full year of its availability in this country, for a rate of 65 reports per 4.5 million prescriptions, or 14.4 reports per million prescriptions. In the first two years of marketing of Baycol, which eventually was taken off the market because of an unusually high rate of reports of rhabdomyolysis, there were 42 reports out of 2.8 million prescriptions filled in this country, for a rate of 15 reports per million prescriptions filled. Thus, it appears that Crestor is in the range much closer to the rate of rhabdomyolysis reports for Baycol than that of any other statin.

It becomes clearer by the day that this drug is uniquely toxic without offering any unique benefit, and that it must be removed from the market.

Sincerely,



Sidney M. Wolfe, MD

Director, Public Citizen's Health Research Group